Institute of Experimental Morphology, Pathology and Anthropology with Museum
Bulgarian Anatomical Society

Acta morphologica et anthropologica, 18
Sofia • 2012

Ofuji Papuloerythroderma – a Dermadrome or a Presenting Sign of Cutaneous Lymphoma?

M. Gantcheva, V. Broshtilova, S. Marina**

Institute of Experimental Morphology, Pathology and Anthropology with Museum, Bulgarian Academy of Science, Sofia, Bulgaria
**Department of Dermatology and Venereology, Alexander's University Hospital, Sofia, Bulgaria*

Ofuji papuloerythroderma is a highly pruritic skin eruption that predominantly affects elderly men, and consists of conglomerating flat-topped erythematous papules forming diffuse eryhtroderma, which spares only the skin folds to produce the so-called "deck-chair sign". A 56-year-old white man with classic manifestation of Ofuji papuloerythroderma is presented. Immunohistochemical and molecular studies of the affected peripheral lymph nodes detected primary cutaneous T-cell lymphoma of low grade malignancy and raised questions as to the nosologic implications of the papuloerythroderma. Although it has till recently been referred to as an unusual variant of atopic dermatitis of elderly patients due to the eosinophilia, lymphopenia, high total serum IgE levels, and positive specific IgE radioallergosorbent results. it seems more possible papuloerythroderma to be a chronic reactive process to a nowadays unidentified cutaneous antigen, which may evolve into a primary cutaneous T-cell lymphoma. Moreover, a clonal expansion of highly activated CD 3 /-/ CD 4 /+/ aberrant T cells, that were detected in the peripheral blood of our patient, is suggested to produce a large amount of IL-5 thus stimulating the bone marrow eosinophil differentiation. Conclusions that Ofuji papuloerythroderma may either occur as a proceeding paraneoplastic syndrome or a primary cutaneous T-cell lymphoma resulting from the severe chronic skin eruption are made. Hence the problem remains open for further discussion.

Key words: erythroderma, cutaneous T cell lymphoma

Introduction

Ofuji papuloerythroderma (OPE) was first-described by S. Ofuji et al. [20] in 1984. as a highly pruritic skin eruption of erythematous, brownish papules in vast sheets, which spare the skin folds to produce the so-called "deck-chair sign"[5]. The laboratory findings usually reveal hypereosinophilia with lymphopenia, and elevated total IgE serum levels. Peripheral lymphadenopathy is commonly present. In 1987, R. Staughton et al. [27] reported the first Caucasian case of Ofuji papuloerythroderma, who had nail bed and buttock infarctions in addition to the usual signs. Less than 70 cases have been described up to now, most of which affected Asiatic men [25].

This case represents a Caucasian man with a skin eruption of OPE and immunohistochemical and molecular sings of primary cutaneous T-cell lymphoma.

Case Report

A 56-year old man presented with a 7-month history of extremely pruritic exfoliative dermatitis, unresponsive to topical steroids and oral antihistamines. He had lost 8 kg for the last 7 months, and suffered enormous fatigue. No past history of atopy or potentially causative drug intake was incriminated. The physical examination showed generalised dermatosis of lichen planus-like erythematous excoriated or flat-topped papules that spare the body folds causing the so-called "deck-chair sign". The papular rash appeared to follow the Langer's lines on the lateral aspects of the trunk. Diffuse well-demarcated brown-yelowish palmo-plantar hyperkeratosis was seen. Peripheral bilateral cervical and axillar lymphadenopathy of firmly elastic conglomerated nodules, 5 cm in diameter, were present.

Abnormal laboratory findings included eosinophilia [21%, normal<15%], lymphopenia [11%, normal: 20-40%] and increased total IgE serum level [980 U/ml, normal <300U/ml]. No Sezary cells were present in the peripheral blood count. HIV, Hepatitis A, B, and C serologic tests were negative.

The histology findings showed orthohyper- and parakeratotic epidermis with focal spongiosis. A diffuse dermal interstitial and perivascular infiltrate of predominantly eosinophils and lymphocytes was present under an intact Grenz zone (Fig.1). A diffuse

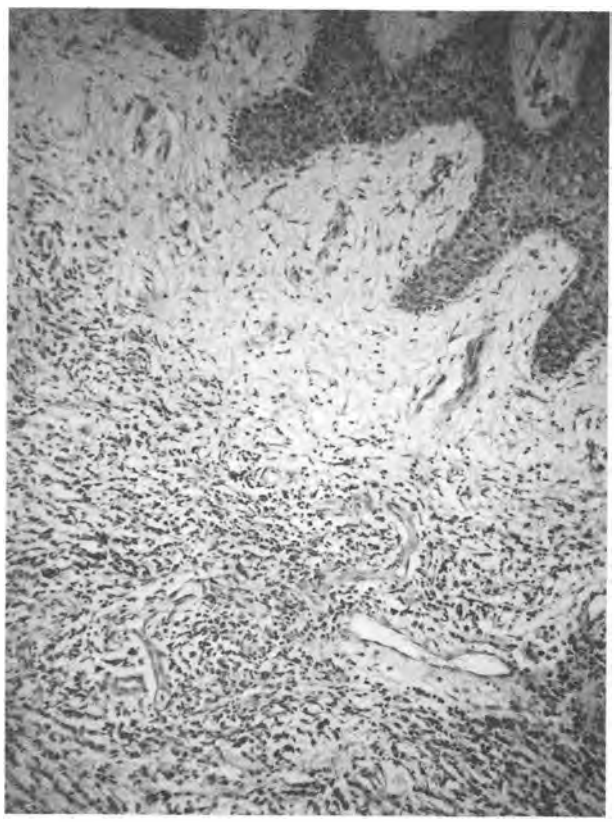

Figure 1. A heavy perivascular infiltrate of predominantly eosinophils under an intact Grenz zone

polymorphous well-vascularized infiltration of large lymphoid cells, plasma cells and eosinophils destroyed the normal structure of the inguinal lymph node. CD3+ (Fig.2), CD4+ and CD8- populations were detected immunohistochemically. Abnormal monoclonal proliferation of atypical CD 3- CD 4+ T cells was detected with peripheral blood flow cytometry.

Upper gastrointestinal endoscopy showed duodenal bulb erosion with no sings of active bleeding. Chest X-ray study, abdominal ultrasound, thorax and abdominal computer tomography scans failed to detect any deep node or visceral involvement. No parasites were detected in the stool samples.

Based on the histology findings, diagnosis of OPE, with immunology and molecular features of primary cutaneous T-cell lymphoma, was concluded. Systemic 6-Methylprednisolon [initial dose of 48mg daily], and azathioprin [100 mg/ day] were administered. Significant improvement occurred at the third month of therapy, when the immuno supressor was discontinued, and the corticosteroid gradually tapered to a continuing treatment of 8 mg per day. The first-year routine follow-up showed flattening of the lesions with less-marked erythema.

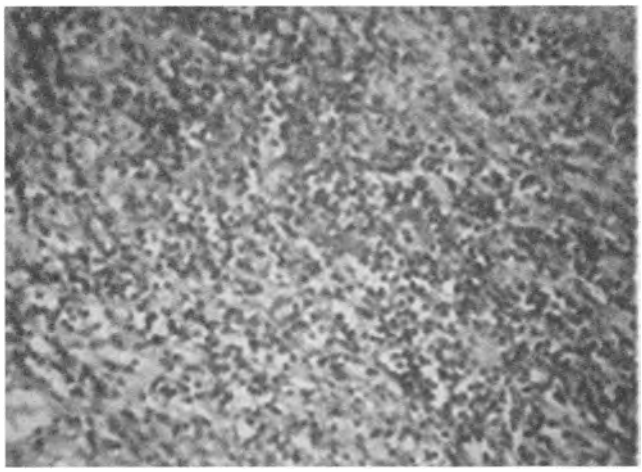

Figure 2. CD 3+ lymphoid infiltrate destroyed the normal lymph node architecture.

Discussion

OPE is a chronic dermatosis, that predominantly affects elderly men, and consists of conglomerating flat-topped erythematous papules forming diffuse eryhtroderma, which spares only the skin folds- the so-called "deck-chair sing". An unknown circulatory eosinophilic factor [14, 16] or a vascular block due to a subsequent immune reaction are suggested to cause the fold sparing [32]. Intense pruritus, lymphopenia, and hypereosinophilia remain constant features, while asymptomatic axillar and inguinal lymphadenopathy, palmoplantar hyperkeratosis, signs of nail bed infarction, and an increase of total serum IgE are less commonly present [3,9,31]. Peripheral CD4 deficiency is also found [33] and thrombocytopenia was once reported [4]. The histology findings are non-specific, usually showing slightly acanthotic epidermis with focal spongiosis [9], and a dense perivascular infiltrate of lymphocytes, histiocytes, plasma cells, and eosinophils in the upper and mid-dermis.

Nosographic siting of OPE is still under discussion [23]. It is referred either as an unusual variant of atopic dermatitis of elderly patients due to the eosinophilia, lymphopenia, high total serum IgE levels, and positive specific IgE radioallergosorbent results [25], or as a reactive process to a nowadays unidentified cutaneous antigen [7,9] in the view of T-helper cell excess and Langerhans cells proliferation. C.Bachmeyer et al. [3] even suggested that OPE could be an initial manifestation of hypereosinophilic syndrome.

Lymphomas [2,4,8,15,22,23,26,28,30], visceral tumours [1,17,18,19], fungal infections [21,31] parasites [10] and HIV infection [6] have been found to coexist with OPE, however, their association may be highly accidental [25].

Recently, it is hypothesise that a chronic reactive inflammation of the skin caused by a certain antigen may evolve into a primary cutaneous T-cell lymphoma. Moreover, a clonal expansion of highly activated CD 4 /+/ T cells is suggested to produce a large amount of IL-5 for stimulating bone marrow eosinophil differentiation [11]. Circulating T cells with an aberrant immunophenotype CD3/-/ CD4/+/ or CD3/+/ CD4/-/ CD8/-/ can be associated with different forms of skin inflammation such as hypereosinophilic syndrome, and leukemic T cell lymphoma [13]. A recent study of 26 patients with cutaneous T-cell lymphoma showed elevation of eosinophilic markers of activation as eotaxin, eosinophil peroxidase, and IL-5 in 14 patients, all of which have suffered peripheral eosinophilia [12]. Ten of these patients died within few months, which proved a significant positive correlation between peripheral eosinophilic count and poor clinical prognosis of T-cell lymphoma. In vitro investigations on the lymphoma susceptibility to glucose oxidase have shown that high deposits of eosinophil peroxidase decrease its therapeutic effect [23]. Therefore, peripheral eosinophilia is already referred to as a bad prognostic factor to cause therapeutic refractivity and high mortality in patients with cutaneous lymphomas.

Conclusion

This case represents an OPE that either occur as a proceeding paraneoplastic syndrome or a primary T-cell lymphoma resulting from the severe chronic skin eruption. However, the problem remains open for further discussion.

References

1. Akioka J, Moriwaki S, Yagi H, et al. A case of papuloerythroderma: an association with early cancer. Arch dermatol 1991; 127: 96-98.
2. Aste N, Fumo G, Conti B. Ofuji papuloerythroderma. J Eur Ac Dermatol Venereol 2000; 14: 55-57.
3. Bachmeyer C, Petit A, Nahmias M, et al. Papuloerythrodermie d'Ofuji. Aspect clinique d'un syndrome hypereosinophilique? J Ann Dermatol Venereol 1991; 118: 895-897.
4. Dwyer C, Chapman R, Smith G. Papuloerythroderma and cutaneous T-cell lymphoma. Dermatology 1994; 188: 326-328.
5. Farthing C, Staughton R, Harper J, et al. Papuloerythroderma-a further case with the deck-chair sign. Dermatologica 1986; 172: 65-66.
6. Garcia-Patos V, Repiso T, Rodrigues-Cano L, et al. Ofuji papuloerythroderma in a patient with the acquired immunodeficiency syndrome. Dermatology 1996; 192: 164-166.
7. Greer J, York J, Cousar J, et al. Peripheral T-cell lymphoma: a clinicopathologic study of 42 cases. J Clin Oncol 1984; 2: 788-798.
8. Grob J, Collet-Villette A, Horchowski N, et al. Ofuji papuloerythroderma. Report of a case with T-cell lymphoma and discussion of the nature of this disease. J Am Acad Dermatol 1989; 20: 927-931.

9. Harris D, Spencer M, Tidman M. Papuloerythroderma-clinical and ultrastructural features. Clin Exp Dermatol 1990; 15: 105-106.
10. Hasegawa W, Tachibana T, Ho K, et al. Papuloerythroderma of Ofuji associated with strongyloidiasis. J Dermatol 2003; 30: 157-158.
11. Hautmann C, Gratzl S. Simon D, et al. Cytokine-producing lymphoma T cells in the skin and peripheral blood associated with atopy and hyperoesinophilia. Hautarzt 1999; 50: 743-747.
12. Ionescu MA, Rivet J, Morel P, Janin A. In situ eosinophil activation in 26 cases of primary cutaneous T-cell lymphomas with blood hypereosinophilia. Ann Dermatol 2002; 6: p.2378.
13. Kitano K, Ichikawa N, Shimodaira S, et al. Eosinophilia associated with clonal T-cell proliferation. Leuk Lymphoma 1997; 27: 335-342.
14. Langtry J, Rowland PC, Harper J, et al. Papuloerythroderma in a woman. J R Soc Med 1985; 81: 170-171.
15. Makajima M, Hashikawa Y, Komatsu Y, et al. Leukemic T-cell lymphoma with lichen ruber-like erythroderma. Rinsho Derm (Tokyo) 1988; 30: 1523-1527.
16. Mojzes J, Schneider I. Papuloerythroderma Ofuji with an unusual features. Eur J Dermatol 1995; 5: 36-39.
17. Nazzaki G, Sabattini C. Ofuji's papuloerythroderma. An association with early gastric cancer. Eur J Dermatol 1999; 9: 317-318.
18. Nishijima S. Papuloerythroderma associated with hepatocellular carcinoma. Br J Dermatol 1998; 139: 1115-1116.
19. Ofuji S. Papuloerythroderma. J Am Acad Dermatol 1990; 22: p.697.
20. Ofuji S, Furukawa F, Miyachi Y, et al. Papuloerythroderma Ofuji. Dermatologica 1984; 169: 125-130.
21. Ohnishi K, Nagai Y, Katsuyuki O, et al. Primary cutaneous histoplasmosis in papuloerythroderma (Ofuji). J Dermatol 1994; 21: 586-589.
22. Pereiro M, Sanchez-Aguilar D, Pereiro-Ferreiros M, et al. Cutaneous T-cell lymphoma: an expression of papuloerythroderma of Ofuji. J Eur Ac Dermatol Venereol 2003; 17: 240-241.
23. Samoszuk MK, Nguyen V, Thomas CT, et al. Effects of sonicated eosinophils on in vitro sensitivity of human lymphoma cells to glucose oxidase. Cancer Res 1994; 54: 2650-2653.
24. Saurat JH. Papuloerythroderma. Disease or pattern? Dermatology 1993; 186: p. 163.
25. Schepers C, Malvehy J, Azon-Masoliver A, et al. Papuloerythroderma of Ofuji: a report of 2 cases including the first European case associated with visceral carcinoma. Dermatology 1996; 193: 131-135.
26. Shah M, Reid WA, Layton AM. Cutaneous T cell lymphoma presenting as papuloerythroderma: a case and review of the literature. Clin Exp Dermatol 1995; 20: 161-163.
27. Staughton R, Langtry J, Rowland PC, et al. Papuloerythroderma- the first European case. In: Wilkinson DS, Mascaro JM, Orfanos CE, eds. Clinical dermatology. The CMD case collection. World Congress of dermatology, Berlin, Schattauer, 1987: 181-182.
28. Suh K, Kim H, Chae Y, et al. Ofuji papuloerythroderma associated with follicular mucinosis in Mycosis fungoides. Dermatology 1998; 25: 186-189.
29. Takiguchi Y, Shimada K, Suzuki M, et al. A case of B-cell lymphoma proceeded by papuloerythroderma (Ofuji). Jpn J Clin Dermatol 1987; 30: 1523-1527.
30. Tay Y, Tan K, Ong B. Papuloerythroderma of OFuji and cutaneous T-cell lymphoma. Br J Dermatol 1997; 137: 160-161.
31. Tay Y, Tan K, Wong W, et al. Papuloerythroderma of Ofuji: a report of three cases and a review of the literature. Br J Dermatol 1994; 130: 773-776.
32. Wakeel RA, Keete M, Chapman RS. Papuloerythroderma: another case of a new disease. Arch Dermatol 1991; 127: 96-98.
33. White T, Langtry J, Beetham R, et al. CD8 deficiency in papuloerythroderma: in Poulik MD et al eds. Protides of the Biological Fluids. Oxford, Pergamon 1989, vol. 36, pp. 303-312.